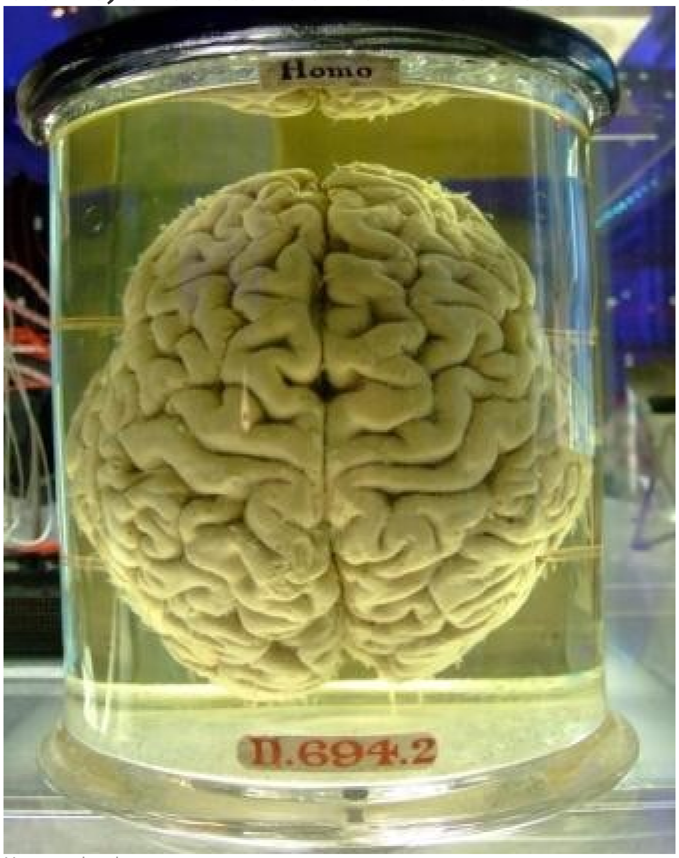
New research points to an ancient energy tradeoff that meant more fuel for brains, and less fuel for muscles.



Human brain

Recently while visiting the National Museum of Natural History in Washington, D.C., I found myself pondering the noggins of some very, very, old apes.

Along one wall of the Hall of Human Origins — an exhibit on human evolution that opened in 2010 — were 76 fossil skullsfrom 15 species of early humans. Looking at these skulls, one thing was clear: millions of years of evolution have given us much bigger brains.

In the 8 million to 6 million years since the ancestors of humans and chimps went their separate ways, the human brain more than tripled in size. If the earliest humans had brains the size of oranges, today's human brains are more akin to cantaloupes.

As for our closest primate relatives, the chimps? Their brains haven't budged.

With our big brains we compose symphonies, write plays, carve sculptures and do math. But our big brains came at a cost, some scientists say.

In two recent studies, researchers from Duke University suggest the human brain boost may have been powered by a metabolic shift that meant more fuel for brains, and less fuel for muscles.

Our big, hungry brains

Co-author Olivier Fedrigo told me the full story one morning over coffee near his home in Durham, North Carolina. The human brain isn't just big, he explained. It's also hungry.

While the brain makes up only 2% of our body mass, it consumes more than 20% of our oxygen supply and blood flow. Compare that to only 7-8% in other primate species, Fedrigo said.

The human brain uses more energy, pound for pound, than any other tissue. Yet our body burns the same number of calories as other primates our size.

In 1995, two researchers in the U.K. published a landmark study arguing that if our overall energy budget didn't go up, our bodies must have compensated by diverting energy from somewhere else. The theory is called the expensive tissue hypothesis, first proposed by anthropologist Leslie Aiello, then of University College London, and physiologist Peter Wheeler of Liverpool John Moores University in England.

In the years after Aiello and Wheeler published their paper, the expensive tissue hypothesis started to gain support, though scientists had different ideas about which tissues paid the price for bigger brains. "There's been a lot of debate about how this tradeoff might have been accomplished," said Duke evolutionary biologist Greg Wray.

Brains versus brawn, paleo style

Bodybuilder

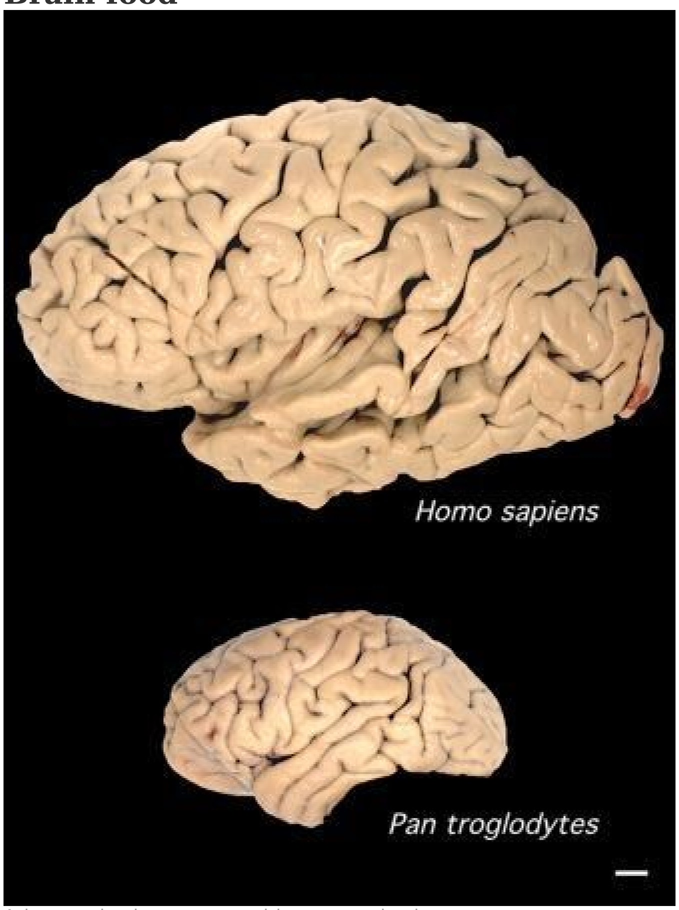
In 2003, an anthropologist at Northwestern University named William Leonard published a study arguing that the price we paid for a bigger brain may have been punier muscles. "[The thinking was that] even if you're totally buff, you're nothing compared to a chimp," Wray said.

Subsequent studies have raised questions about whether humans are really the scrawny members of the primate clan. Rather than having less muscle than would be expected for an ape of our size, it may be that our muscle is just distributed differently, said Duke anthropologist Christine Wall. Compared with other primates "humans are scrawny up top but bulky below," she said.

"But the hypothesis still holds," Fedrigo added. To build a bigger brain at the expense of muscle, "our muscles could have evolved to be smaller, or more efficient, or the metabolic cost of walking could have decreased, or it could have been some combination of these things," he said. "The possibilities aren't mutually exclusive."

In a study published last October, Fedrigo, Wray, Wall and colleagues tested the tradeoff hypothesis and pinpointed changes in two groups of molecules that may have shuttled more energy to our brains, and less to our muscles. "This is the first time the hypothesis has been tested at the molecular level," Wray told attendees at the 2011 meeting of the American Association for the Advancement of Science.

Brain food



A human brain versus a chimpanzee brain.

The primary source of energy for the brain is glucose, which is pumped into cells where it is needed most with the help of proteins called glucose transporters. Glucose transporters are encoded by a family of about a dozen genes. The researchers zeroed in on two glucose transporter genes, one of which, called

SLC2A1, is turned on mostly in brains, and the other, called SLC2A4, is turned on mostly in muscles.

Mutations in SLC2A1 lead to insufficient glucose getting across the blood-brain barrier, which can cause seizures, learning disabilities, or a condition called microcephaly, which turns a normal brain into a tiny one. “The brain basically starves,” Wray said.

To get a better picture of how these genes evolved after humans and other primates went their separate ways, the researchers compared the human versions of the genes with the same genes in chimps and two more distantly related primates, orangutans and macaques. When they compared the DNA sequences of the genes from each species, they found a number of changes in the human version of each gene but not the other three species.

To find out if those changes may have helped to ferry more glucose to brains, and less to muscles, they measured the amount of mRNA copies of each gene — a measure of how much protein the gene is likely to make — in brain, muscle, and liver samples from each species. Compared with chimps, humans make three times more of the glucose transporter found in brains, but only 60% of that found in muscles.

“The tradeoff is exactly what one might predict,” Wray said.

These probably weren’t the only tradeoffs that led to our enlarged brains, the researchers say. In another study published last year, they pinpointed another set of genes that may have funneled more energy to brains, and less to muscles — this time in the form of a metabolite called creatine. Glucose is the brain’s primary fuel, but creatine provides a backup source of quick-burn energy when glucose runs low.

Creatine is ferried in and out of cells with the help of several genes. When the researchers measured the expression levels of these genes in tissue samples from humans, chimps and macaques, they found that human brains had twice the levels of SLC6A8 and CKB, two genes that regulate how creatine is used by cells. But in contrast to brains, the levels in human muscles were no different from chimps.

Back at the Hall of Human Origins, I turned away from the wall of skulls and made my way to another part of the exhibit, where lifelike busts of eight early humans, outfitted with muscles, flesh and hair, stare out from their cases.

“Meet your ancestors,” a sign on the wall read.

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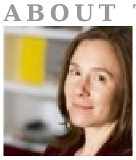

Robin Anne Smith

- Robin Smith taught writing at Duke University for four years before joining the news room at the National Evolutionary Synthesis Center in Durham, North Carolina, where she writes about life in the deep sea, atop the world's highest mountains, and everywhere in between. Robin earned a PhD in evolutionary biology in 2005, and has published academic articles in *Evolution, American Naturalist*, and the *American Journal of Botany*. She has also written for the *Raleigh News and Observer*, the *Charlotte Observer*, and the blog column of *Scientific American*. Robin is a member of the National Association of Science Writers, and serves on the board of the local science writing group, Science Communicators of North Carolina. When she's not at her desk, Robin spends her time dancing, hiking, and learning the secrets of homemade sorbet. She tweets at @NESCent and (more rarely) @robinannsmith. Profile photo by Jon Gardiner.

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